Misregulated Mitophagy in Parkinsonian Neurodegeneration

Grant Award Details

Misregulated Mitophagy in Parkinsonian Neurodegeneration

Grant Type: Basic Biology V

Grant Number: RB5-06935

Project Objective: To understand the regulatory mechanisms controlling mitochondrial function, transport and clearance, as well as the mechanisms by which even subtle disturbances of these processes may contribute to neurodegeneration. The aims proposed in the project are the first steps toward probing the relevance of misregulated mitochondrial clearance via mitophagy to Parkinsonian neurodegeneration. The project will investigate the central hypothesis is that in Parkinson's disease mutant cells, mitophagy is impaired thereby leading to accumulation of oxidative stress and neurodegeneration.

Investigator:

Name:	Xinnan Wang
Institution:	Stanford University
Type:	PI

Disease Focus: Parkinson's Disease, Neurological Disorders

Human Stem Cell Use: iPS Cell

Award Value: $1,174,943

Status: Active

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Misregulated Mitophagy in Parkinsonian Neurodegeneration

Public Abstract: Parkinson's disease (PD), is one of the leading causes of disabilities and death and afflicting millions of people worldwide. Effective treatments are desperately needed but the underlying molecular and cellular mechanisms of Parkinson's destructive path are poorly understood. Mitochondria are cell's power plants that provide almost all the energy a cell needs. When these cellular power plants are damaged by stressful factors present in aging neurons, they release toxins (reactive oxygen species) to the rest of the neuron that can cause neuronal cell death (neurodegeneration). Healthy cells have an elegant mitochondrial quality control system to clear dysfunctional mitochondria and prevent their resultant devastation. Based on my work that Parkinson's associated proteins PINK1 and Parkin control mitochondrial transport that might be essential for damaged mitochondrial clearance, I hypothesize that in Parkinson's mutant neurons mitochondrial quality control is impaired thereby leading to neurodegeneration. I will test this hypothesis in iPSC (inducible pluripotent stem cells) from Parkinson's patients. This work will be a major step forward in understanding the cellular dysfunctions underlying Parkinson's etiology, and promise hopes to battle against this overwhelming health danger to our aging population.

Statement of Benefit to California: Parkinson's disease (PD), one of the most common neurodegenerative diseases, afflicts millions of people worldwide with tremendous global economic and societal burdens. About 500,000 people are currently living with PD in the U.S, and approximate 1/10 of them live in California. The number continues to soar as our population continues to age. An effective treatment is desperately needed but the underlying molecular and cellular mechanisms of PD's destructive path remain poorly understood. This proposal aims to explore an innovative and critical cellular mechanism that controls mitochondrial transport and clearance via mitophagy in PD pathogenesis with elegant employment of bold and creative approaches to live image mitochondria in iPSC (inducible pluripotent stem cells)-derived dopaminergic neurons from Parkinson's patients. This study is closely relevant to public health of the state of California and will greatly benefit its citizens, as it will illuminate the pathological causes of PD and provide novel targets for therapuetic intervention.